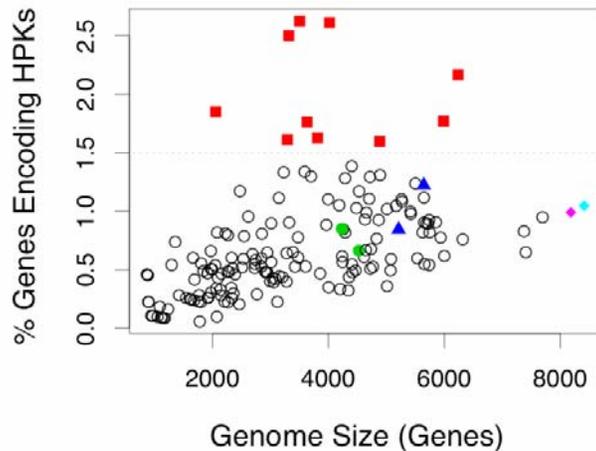


Introduction

Two-component systems including histidine protein kinases represent the primary signal transduction paradigm in prokaryotic organisms. To understand how these systems adapt to allow organisms to detect niche-specific signals, we analyzed the phylogenetic distribution of nearly 5000 histidine protein kinases from 207 sequenced prokaryotic genomes. We found that many genomes carry a large repertoire of recently evolved signaling genes, which may reflect selective pressure to adapt to new environmental conditions. Both lineage-specific gene family expansion and horizontal gene transfer play major roles in the introduction of new histidine kinases into genomes; however, there are differences in how these two evolutionary forces act. Genes imported via horizontal transfer are more likely to retain their original functionality as inferred from a similar complement of signaling domains, while gene family expansion accompanied by domain shuffling appears to be a major source of novel genetic diversity. Family expansion is the dominant source of new histidine kinase genes in the genomes most enriched in signaling proteins, and detailed analysis reveals that divergence in domain structure and changes in expression patterns are hallmarks of recent expansions. These results lead us to conclude that in the ongoing evolution of bacterial signal transduction machinery, some organisms serve as 'producers' generating novel genetic diversity, while others serve as 'consumers' capitalizing on the existing diversity of their peers.



HPKs From Horizontal Gene Transfer

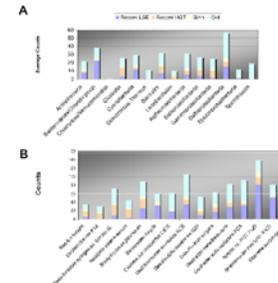
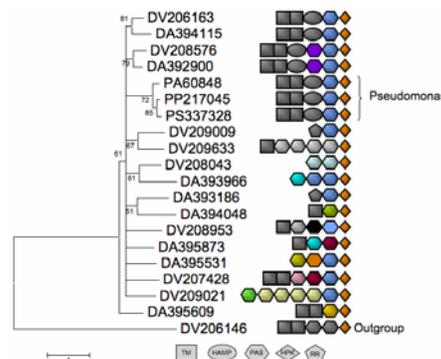
Generate phylogenetic outgroups for each target genome



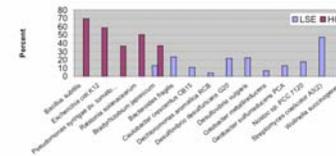
HPK domain pairwise distances



HPKs From Lineage-specific expansion

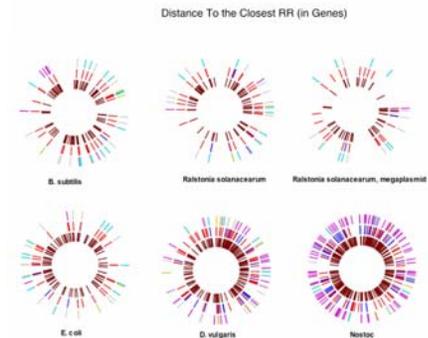
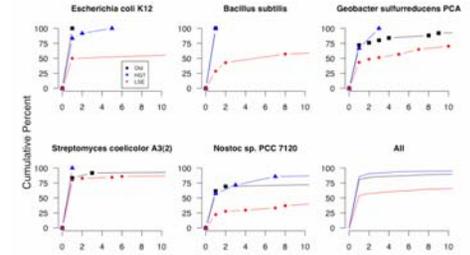


Summary of evolutionary events. The number of events inferred for different bacteria is summarized in this figure. (A) Average numbers for the major taxonomic groups used in this study. (B) Specific numbers for targeted genomes (those with colored symbols in Figure 1). Genomes highlighted as having an unusually large number of new HPKs are observed to have undergone a large number of 'LSE' events.

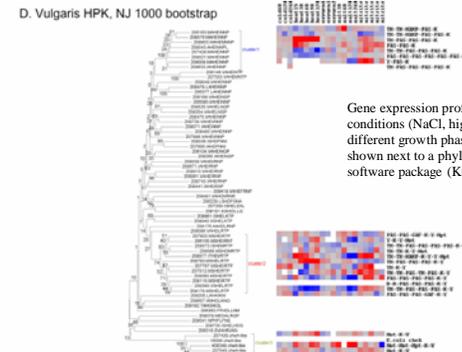


The fraction of HPKs with conserved upstream domains are shown for those genomes rich in HGT events, and the fraction of LSE genes with conserved upstream domains are shown for those genomes rich in LSE.

Proximity of different classes of HPKs to response regulators.



Genomic distribution of HPKs and RRs. The position of signaling proteins in several genomes is shown. In the outer ring, HPKs of different classes are shown: Old (gray), LSE (purple), HGT without duplication (blue), ORFan (green). The middle ring shows the position of response regulators with blue colors indicating hybrid response regulators (containing HPK domains). The inner ring shows the location of all genes in each genome annotated as signaling proteins according to the MicrobesOnline database (Alm et al. 2005a).



Gene expression profiles across a compendium of experimental stress response conditions (NaCl, high/low pH, heat shock, cold shock, nitrite/nitrate, oxygen, and different growth phases) were monitored using DNA microarrays (Alm et al. 2005b), and shown next to a phylogenetic NJ tree (with 1000 bootstraps, generated using the MEGA3 software package (Kumar et al. 2004)) of all HPK domains in *D. vulgaris*.

Acknowledgements

ESPP is part of the Virtual Institute for Microbial Stress and Survival supported by the U. S. Department of Energy, Office of Science, Office of Biological and Environmental Research, Genomics Program:GTL through contract DE-AC02-05CH11231 between Lawrence Berkeley National Laboratory and the U. S. Department of Energy.